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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/852,966	05/10/2001	Rima Kaddurah-Daouk	AVZ-020CN	5588

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EXAMINER	
KIM, VICKIE Y	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 10/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/852,966	KADDURAH-DAOUK, RIMA	
	Examiner	Art Unit	
	Vickie Kim	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *68-70,72,73,75-85 and 88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *68-70,72,73,75-85 and 88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

112 1st rejection-New Matter

Applicant's arguments(i.e. support for creatine monohydrate found at page 30, line 10), filed July 11, 2005, have been fully considered and are persuasive. The112 1st rejection (New Matter) has been withdrawn hereinafter.

103 Rejection

Applicant's arguments have been fully considered but they are not persuasive. Applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made. Further, they do not show how the amendments avoid such references or objections.

a. Yu et al in view of kaddurah-Daouk et al.

Applicant argues that Yu et al fails to teach or suggest administering an effective amount of creatine to the skin of a subject who is suffering from skin disorder associated with free-radicals, aging, sun radiation, stress or fatigue, as claimed by applicant. Yu et al is limited to treatment methods including effective amounts of alpha-hydroxy acids, not methods using effective amounts of creatine compounds as claimed by applicant.(see remarks at page 4, lines 6-11).

Examiner disagrees.

Yu et al clearly teaches administering an effective amount of creatine compounds(as an essential agent for the patented invention of wrinkle or aging symptom treatment) to the patient who is suffering from skin changes associated with aging, see abstract and examples. Applicant's argument which allegedly states that Yu et al's teaching is limited to methods including effective amounts of alpha-hydroxy acids, not methods using effective amounts of creatine compounds as claimed by applicant, is not so critical because the claims are not particularly drawn to a treating skin conditions(e.g. aging) using an therapeutically effective amount of creatine(as an only active agent), but drawn to **administering an effective amount of creatine to the skin of a subject** who is suffering from skin disorder associated with aging as claimed by applicant , where the scope of instant claims are broader than what applicant argues.

It is noted that, the claims must be given their broadest reasonable interpretation. Therefore, the interpretation of claims (i.e. administering an effective amount of creatine compounds to the skin of the patient effective amount of creatine to the skin of a subject who is suffering from skin disorder associated with aging as claimed by applicant) should be made based on the full definition wherein It is clearly taught or suggested by patentee.

For the same reason, applicant's argument (i.e. Le Fur et al fails to teach or suggest any methods using ATP generating system alone, see remarks at page 4, last paragraph) is not persuasive. Le fur et al teach or suggest the claimed invention because Le fur et al teach that a cosmetic composition containing ATP generating

agent(e.g. creatine) is effectively applied to the skin of subject who suffers from skin changes associated with aging such as wrinkles, etc.

Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

Secondary references (Kaddurah-Daouk et al or Carniglia) teaches energy balance(e.g. increasing energy, sustaining energy or modulating energy) in the skin cell controlled by creatine, creatine analogs, and pharmaceutically acceptable salts thereof, see previous office action. As notoriously known by skilled artisan, creatine monohydrate or creatine citrate is a pharmaceutically acceptable creatine salts which are commonly substituted for creatine in the pharmaceutical industries. And thus, the claimed invention is clearly suggested when these references are taken together and the teaching of these references together renders the claimed invention obvious and not patentably distinct over prior art of the record.

Obvious type- Double Patenting(DP) Rejection

As noted by applicant in the remarks(see page 5), the terminal disclaimer(TD) to obviate DP rejection will be filed upon an indication of allowable subject matter, if

appropriate. Thus, the discussion will not be necessary at this point. The rejection is maintained until proper TD is filed.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 68-70, 75-80 and 84-85 are rejected under 35 U.S.C. 103(a) as obvious over Yu et al(US5,702,688) in view of Kaddurah-Daouk et al(US US5324731 and WO9614063).

Claims are drawn to a method for increasing energy reserve, sustaining energy production and modulating energy flow in the skin comprising administering an effective amount of creatine or a salt thereof to a subject who is suffering from skin disorder(e.g. wrinkles) which is associated with free-radicals, aging, sun radiation, stress or fatigue.

Yu et al (US'688, hereinafter) teaches a treatment of abnormal skin conditions(skin aging, wrinkles, psoriasis, etc) using an amphoteric composition comprising an effective amount of creatine or creatinine as an amphoteric compound, see abstract; claim 1; column 34, line 7 and examples.

Applicant's claims differ in that the claims require increasing energy reserve, sustaining energy production and modulating energy flow in the skin.

However, it would have been obvious to one of ordinary skill in the art at that time of the invention was made to use a creatine compound to the subject suffering from skin aging and wrinkles expecting a cell energy balance when Yu et al(US'688) is taken in view of Kaddurah-Daouk et al(US US5324731 and WO9614063).

Firstly, Kaddurah-Daouk et al(US'731 hereafter) teach a creatine(or its salts) and it's use in the treatment of metastasis of epithelial cells via modifying energy level, see column 19, lines 25-42 (e.g. increasing energy reserve, sustaining energy production and modulating energy flow). US'731 teaches energy balance using creatine kinase in the treatment of other diseases such as psoriasis, wound healing, neurological disorders and cerebrovascular diseases, see column 49, lines 30-41

Secondly, Kaddurah-Daouk et al(WO'063, hereinafter) teach a treatment of diseases(e.g. neurological diseases) which are caused by abnormalities in an energy state, wherein the induction or inhibition of creatine kinase is a cause or a consequence of disease and modulating its activity would modulate energy flow and affect cell function. WO'063 teaches that CK(creatine kinase)system is involved in energy buffering/energy transport activities and also involved in ADP and ATP levels intracellularly as well as ADP/ATP ratios. WO'063 specifically teaches that creatine (or its salts) is used for modifying energy of cells in stress via increasing energy reserve, sustaining energy production and modulating energy flow, see abstract and claims, especially page 39, line 8- page 40, line 9 and claim 4. WO'063 teaches various routes

of administration including oral and topical application and dosage regimen, see page 33, lines 1-14. WO'063 teaches enhancement of therapeutic efficacy by co-administering beneficial secondary additives such as Q10 or nicotinamide that attenuate ATP depletion produced by malonate in vivo, see page 42, lines 7-13. WO'063 also teaches a secondary additives such as vitamins,see page 33, line 21.

When these references are combined together, the underlying mechanism(i.e. modulating skin cell energy using creatine compounds) is clearly present in the treatment of skin aging and wrinkle by administering a creatine compound, taught in Yu et al's reference.

It is noted that creatine is also found in skin cell as well as brain, heart and muscle cells that is conventionally known knowledge* at the time of the invention was made(*see PTO-892 for the evidence). It is readily apparent to any skilled artisan that the energy level modification by creatine supplement is not limited to the only brain, muscle or heart cells but any cells that are associated with creatine kinase/creatine phosphate energy system. Thus, one would have motivated to use a creatine compound to modify intercellular energy (e.g. increasing energy reserve, sustaining energy production and modulating energy flow) in the skin cell to treat the diseases associated with imbalanced creatine kinase level.

Thus, the claimed subject matter is not considered to be novel and not patentably distinct over the prior art of the record.

3. Claims 68-70, 75-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Le Fur et al(US 5,256,649) in view of Carniglia (US 4,871,718) and Kaddurah-Daouk et al(US 5,321,030 or WO9614063).

Le Fur(US'649, hereinafter) teaches a cosmetic composition comprising ATP generating system for counteracting skin aging, see abstract. US'649 also teaches that "ATP generating system" refers to any biological extract which is capable of increasing the respiratory cellular activity within mitochondria thus accelerating the cellular metabolism and ATP is generated.

Applicant's claims differ because they require creatine(or its salts).

However, it would have been obvious to one of ordinary skill in the art to substitute ATP generating system with creatine(or its salts) when Le Fur is taken in view of Carniglia(US '718) and Kaddurah-Daouk et al(US'030 or WO'063) because bothCarniglia and Kaddurah-Daouk et al 's patents together remedy the deficiencies of LeFur's.

First, Carniglia(US'718) teaches ATP is generated by creatine phosphate. Secondly, US'030 or WO'063 also teach that creatine or its analogs modulates the energy level in the skin cells via ATP utilization, see column 7, lines 45=60.

One would have been motivated to make such substitution because creatine is easy to obtain and is proven for its efficacy and safety as being a effective precursor for phosphocreatine in vivo.

It is noted again that the modification of cellular energy level via increasing energy reserve, sustaining energy production and modulating energy flow is inherently

possessed feature where the intracellular energy metabolism in skin cell is modified by creatine supplement because creatine is also found in skin cell as well as brain, heart and muscle cells as mentioned above in 102 rejection(supra).

Thus, one would have been motivated to do so, with reasonable expectation of success, because it is always desirable to extend the therapeutic modalities to enhance the quality of the treatment(e.g.cost reduction, improvement of effectiveness) and patient compliance that would give more choices to the users(e.g. individualized based on needs and preference). Additionally the techniques and skills are well within the skilled level of the artisan having ordinary skill as suggested by the cited references.

As to the claims 75-88, each patent teaches the critical elements required by the instant dependent claims as mentioned above in 102 and 103 rejection. Thus, the claims are properly included in this rejection.

As to the claims 72-73, where applicant requires creatine monohydrate or citrate as the effective species of the creatine salt, it is readily envisaged to skilled artisan that creatine monohydrate or creatine citrate is encompaseed by the teaching, that is the pharmaceutically acceptable salts of creatine that is suggested by US030 or WO'063 because it is conventional knowledge* that creatine monohydrate or creatine citrate is pharmacologically effective creatine salts due to same pharmacore(responsible for th therapeutic effects), absent evidence to the contrary, see claim 1 (US'030) & claim 4(WO'063), and PTO-892*.

All the claimed subject matters are not considered to be patentably distinct over the prior art of the record.

Thus, all the claims are properly included in this rejection.

Double Patenting

4. Double patenting rejection is maintained due to the reasons of the record(see paper no.10). As requested by applicant in their response(see at page 7 remark section, paper no.11), this issue will be discussed upon a finding of subject matter that is allowable.

Conclusion

1. No claim is allowed. All the pending claims 68-70, 72-73, 75-85 and 88 are properly maintained in the rejection above.

2. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 571-272-0579. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page be reached on 571-272-0602.. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

VICKIE KIM
PRIMARY EXAMINER

Vickie Kim
Primary Patent Examiner
October 3, 2005
Art unit 1618